Tetrahedron 65 (2009) 3704–3710

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Electrogenerated *N*-heterocyclic carbenes: N-functionalization of benzoxazolones

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ARTICLE INFO

Article history:
Received 18 December 2008
Received in revised form 29 January 2009
Accepted 23 February 2009
Available online 3 March 2009

Keywords:
Benzoxazol-2(3*H*)-one
Ionic liquids
Electrogenerated carbene

ABSTRACT

A simple electrochemical procedure for the N-acylation and N-alkylation of benzoxazol-2(3*H*)-ones has been set up via electrolysis of an ionic liquid containing a benzoxazolone followed by addition of saturated or unsaturated anhydrides or alkyl halides. The electrochemically induced N-functionalization of benzoxazol-2(3*H*)-ones works very well in all tested ionic liquids, avoiding the use of volatile organic solvents. The *N*-acyl and *N*-alkyl derivatives of benzoxazol-2(3*H*)-ones were isolated in good to excellent yields; moreover, the ionic liquid has been reused fivefold maintaining the high yield of the products.

1. Introduction

Benzoxazol-2(3*H*)-one heterocycles are considered 'privileged scaffolds' in the design of pharmacological probes. These heterocycles have, in fact, high versatility in chemical modifications, allowing changes to the characteristics of side-chains on a rigid platform; moreover, they have received considerable attention from medicinal chemists, due to their capacity to mimic a phenol or a catechol moiety in a metabolically stable template.[1] Studies designed to determine the mode of the biological action require the synthesis of many derivatives and, in the last twenty years, this class of compounds has led to the discovery of a number of derivatives endowed with anti-inflammatory and analgesic,[2] antitubercular, antibacterial and antimicrobial,[3] and normolipemic[4] effects. Some benzoxazolone derivatives substituted on the 3-position present anticonvulsant activity;[5] usually, functionalization of the nitrogen atom is of interest since the electronic characteristics of this atom can be decisive for the biological activity. Recently it was reported that alkylation of benzoxazol-2(3*H*)-ones and benzothiazol-2(3*H*)-ones gave intermediates for the synthesis of compounds used in pharmacotherapy for their anticocaine activity, as these substituted heterocycles interact with Sigma-1 receptors.[6] Courtois et al. described the syntheses of new fosmidomycin analogues containing the benzoxazolone ring, which present a potential interest in the treatment of malaria.[7]

From the chemical point of view, *N*-acylbenzoxazolones can be regarded as *N*-protected benzoxazolones, as the acyl group can be removed under mild acid or basic or neutral conditions.[8] Moreover, *N*-crotonylbenzoxazolone was successfully used to obtain, in a Michael addition with various ketonic enolates, the *syn* adduct with very high selectivity.[9] The synthesis of *N*-acyl and *N*-alkyl derivatives of benzoxazol-2(3*H*)-ones required the use of bases in organic solvents, for example, using K_2CO_3 in CH_2Cl_2 or DMF under reflux and in the presence of Bu_4NBr as catalyst,[8] or using DABCO, DMA and dibenzylcarbonate at 135 °C;[10] otherwise, using sodium hydride in DMF.[11]

Over the past several years, room temperature ionic liquids (RTILs) have emerged as alternatives to volatile organic compounds (VOCs), due to their physico-chemical properties.[12] In the electrochemical field, the use of ionic liquids permits the removed of the supporting electrolyte necessary for the conductibility of the medium from the solution. Owing to a high ionic conductivity and a wide electrochemical potential window, RTILs can be considered a helpful alternative to conventional systems, i.e., (VOCs)/supporting electrolyte.[13]

In a recent paper we have described a new methodology for the N-acylation of chiral oxazolidin-2-ones in ionic liquids.[14] This protocol contemplates the electrochemical generation of an *N*-heterocyclic carbene by cathodic reduction of an imidazolium cation, the reaction of this singlet carbene[15] as a base with the oxazolidinone and, last, the addition of an acylating agent. Having obtained good results with this methodology, we thought to apply it to the synthesis of molecules (i.e., benzoxazolones), which are very valuable both from the chemical and from the pharmaceutical point of view.

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doi:10.1016/j.tet.2009.02.057

With this in mind and according to our previous investigation on the electrochemical generation of carbenes in the N-acylation of chiral oxazolidin-2-ones, we investigated the N-functionalization of another important class of heterocycles, the benzoxazol-2(3*H*)-ones, by the use of ionic liquids, which act as solvent/electrolyte/probase[16] under very mild conditions.

2. Results and discussion

According to the general purpose for simple experiments, the reactivity of benzoxazol-2(3*H*)-ones versus acylating or alkylating agents was investigated following this procedure: a solution of an ionic liquid containing benzoxazolone was electrolyzed under galvanostatic control in a very simple cell (a beaker equipped with a three hole cap), Pt cathode and anode, at room temperature under N_2 atmosphere. After the consumption of a prefixed number of F mol^{-1} of benzoxazol-2(3*H*)-one (in the optimized condition about 1 h), the current was switched off and the acylating or alkylating agent was added to the cathodic solution; the mixture was stirred at room temperature for 2 h. Workup of the catholite (see Experimental section) provided the corresponding *N*-acyl or *N*-alkyl derivative in elevated yield. The series of ionic liquids used is reported in Figure 1.

To enhance the usefulness of the electrosynthetic methodology, increasing efforts are being devoted to develop as easy as possible electrochemical reaction systems, mainly focused on working under constant current conditions (thus avoiding the use of a reference electrode).[17] For this reason, we carried out all the electrolyses under galvanostatic control; however, it is interesting to see that working under potentiostatic control, the reaction went very well too (see Table 1, entry 2 vs entry 6).

In our previous work, we have suggested that the presence of an *N*-acyloxazolidinone in the cathodic BMIM-BF_4 solution is consistent with the electrochemical reduction of the 1-butyl-3-methyl-1*H*-imidazolium cation to the 1-butyl-3-methyl-1*H*-imidazol-2-ylidene carbene, followed by proton exchange equilibrium between the electrogenerated carbene and the oxazolidin-2-one and subsequent N-acylation of the nitrogen anion.[14]

It is known, in fact, that 1-butyl-3-methyl-1*H*-imidazol-2-ylidene is a singlet carbene and behaves mainly as a nucleophile and a base.[15] Considering that benzoxazol-2(3*H*)-one and 2-oxazolidinone are structural analogous, the mechanism of acylation may be hypothesized to be the same (see Scheme 1). On account of this, as reported in Table 1, the results of the electrolyses under galvanostatic and potentiostatic conditions show excellent results.

Table 1
Electrolyses of solutions of benzo[*d*]oxazol-2(3*H*)-one (**1a**) in various ionic liquids[a] followed by the addition of propionic anhydride **2a** (ρ=1.0)[b] to give 3-propionyl-benzoxazol-2(3*H*)-one (**3aa**)

Entry	Ionic liquid[c]	I (mA cm^{-2})	Q (F mol^{-1})[d]	**1a** [%] (recovered)	Product **3aa** yield[e] [%]
1	BMIM-BF_4	16	1.0	13	73
2	BMIM-BF_4	25	1.0	—	97
3	BMIM-BF_4	35	1.0	19	69
4	BMIM-BF_4	25	1.5	7	89
5	BMIM-BF_4	25[f]	1.0	29	70
6	BMIM-BF_4	−1.9 V[g]	1.0	—	99
7	BMIM-$MeSO_4$	25	1.0	tr	94
8	BMIM-PF_6	25	1.0	—	95
9	BnMIM-BF_4	25	1.0	—	96
10	BDMIM-BF_4	25	1.0	30	64
11	MIM-Cl[h]	25	1.0	100	—

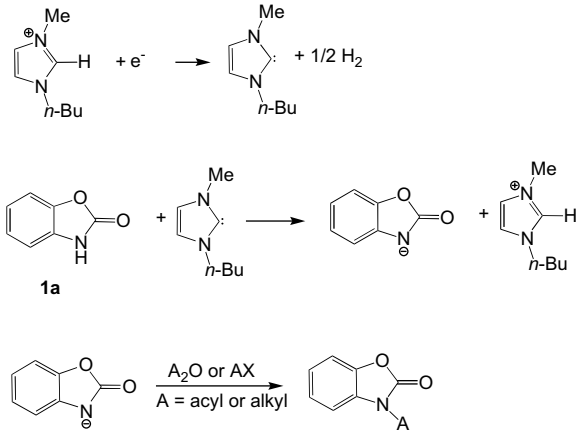
[a] Electrolyses carried out under galvanostatic conditions. Divided cell, Pt anode and cathode, room temperature, N_2 atmosphere.
[b] Molar ratio propionic anhydride/benzoxazolone.
[c] BMIM: 1-butyl-3-methylimidazolium; BnMIM: 1-benzyl-3-methylimidazolium; BDMIM: 1-butyl-2,3-dimethylimidazolium; MIM: 1-methyimidazolium.
[d] Number of Faradays per mole of **1a** supplied to the electrodes.
[e] Isolated yields based on starting **1a**.
[f] Benzo[*d*]oxazol-2(3*H*)-one **1a** was added at the end of the electrolysis.
[g] Electrolyses carried out under potentiostatic conditions versus Ag pseudo reference.
[h] In this ionic liquid the N-acylation of **1a** did not occur, but 1-methyl-3-propionylimidazolium chloride was isolated as product.

To further optimize the experimental conditions, the influence of different parameters on the yields of isolated *N*-acylbenzoxazolone was checked using benzo[*d*]oxazol-2(3*H*)-one **1a** as a model compound in different RTILs. Accordingly, several electrolyses were carried out varying the value of I (current density, Table 1, entries 1–3) and Q (number of Faradays per mole of benzoxazol-2(3*H*)-one supplied to the electrodes, Table 1 entry 2 vs entry 4). The nature of the anion (BF_4^-, PF_6^-, $CH_3SO_4^-$) of the RTIL had no effect on the yields of acylated product, that remain very high in all cases (Table 1, entries 2, 7, 8). The type of substituent on the imidazolium cation can modify the yields: the substitution of the butyl group with a benzyl one led to the same yield of **3aa** (Table 1, entries 9 vs entry 2), while when 1-butyl-2,3-dimethylimidazolium tetrafluoroborate is used **3aa** was isolated in 64% yield (BDMIM-BF_4, Table 1, entry 10 vs entry 2). This can be ascribed to the fact that this particular imidazolium cation is not able to generate a carbene in 2-position; nevertheless, it is reported[18] that the methyl in 2-position is acidic and therefore can be cathodically deprotonated, but with a lower current efficiency. On the other hand, when 1-methylimidazolium

X^-= BF_4^-, PF_3^-, $CH_3SO_4^-$, Cl^-.

	R_1	R_2	R_3
BMIM	*n*-Bu	H	CH_3
BDMIM	*n*-Bu	CH_3	CH_3
BnMIM	$PhCH_2$	H	CH_3
MIM	CH_3	H	H

Figure 1. Ionic liquids used in the N-functionalization of benzoxazol-2(3*H*)-ones.



Scheme 1.

Table 2
Electrochemical synthesis of N-functionalized benzoxazol-2(3*H*)-ones (**3**) according to the optimized conditions (Table 1, entry 2)

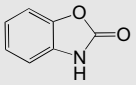
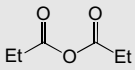
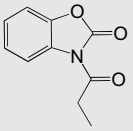
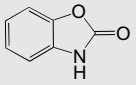
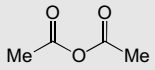
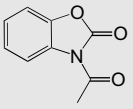
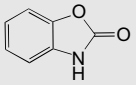
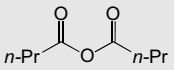
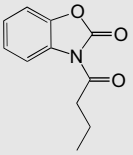
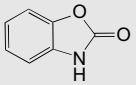
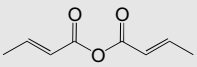
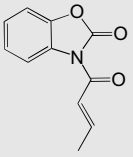
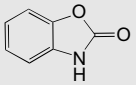
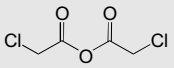
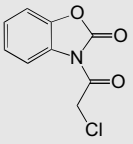
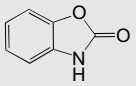
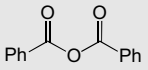
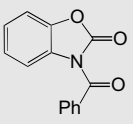
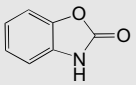
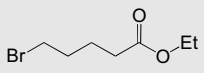
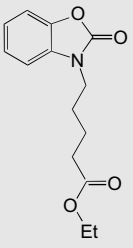
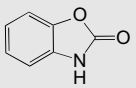
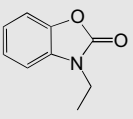
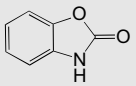
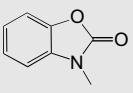
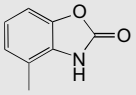
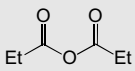
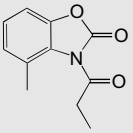
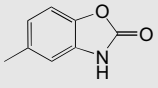
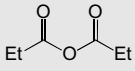
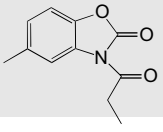
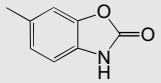
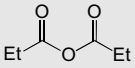
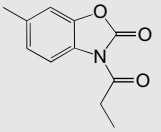
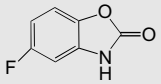
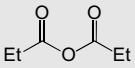
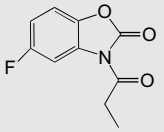
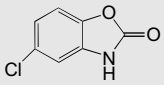
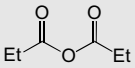
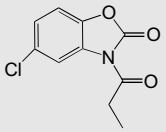
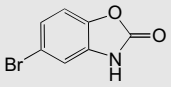
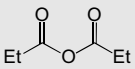
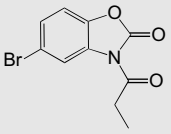
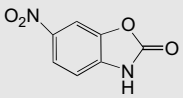
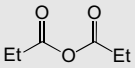
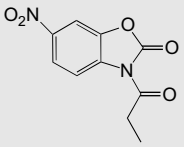
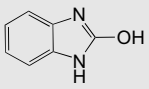
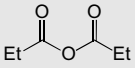
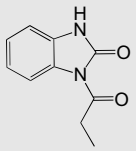
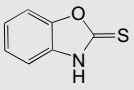
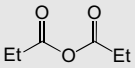
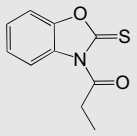
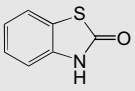
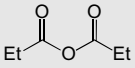
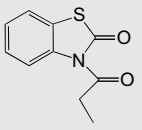
Entry	Benzoxazolones		**2**		Product yield (%)	
1		**1a**		**2a**		**3aa** (89)
2		**1a**		**2b**		**3ab** (97)
3		**1a**		**2c**		**3ac** (85)
4		**1a**		**2d**		**3ad** (87)
5		**1a**		**2e**		**3ae** (70)
6		**1a**		**2f**		**3af** (64)
7		**1a**		**2g**		**3ag** (87)
8		**1a**		**2h**		**3ah** (99)
9		**1a**		**2i**		**3ai** (63)
10		**1b**		**2a**		**3ba** (15)
11		**1c**		**2a**		**3ca** (71)

Table 2 (*continued*)

Entry	Benzoxazolones		**2**		Product yield (%)	
12		**1d**		**2a**		**3da** (98)
13		**1e**		**2a**		**3ea** (79)
14		**1f**		**2a**		**3fa** (81)
15		**1g**		**2a**		**3ga** (78)
16		**1h**		**2a**		**3ha** (55)
17		**1i**		**2a**		**3ia** (70)
18		**1j**		**2a**		**3ja** (25)
19		**1k**		**2a**		**3ka** (14)

chloride (MIM-Cl, Table 1, entry 11) was used, no **3aa** was isolated. This could be due either to the fact that the cathodic deprotonation of the MIM was not at the 2-position, but at the nitrogen atom in 3-position, or that in the case where more than one NH-acid is present in the cathodic solution after electrolysis, there is competition between the reaction of carbene with its parent molecule and carbene with substrate. In fact, only 1-methyl-3-propionylimidazolium chloride was isolated from the cathodic solution (i.e., the reaction product between the 3-nitrogen anion of MIM, and propionic anhydride).

The current density I and charge passed in electrolyses Q influenced drastically the yields of **3aa**; in fact, both a lower and a higher current density (with respect to the optimum value of 97% at 25 mA cm^{-2} Table 1, entry 2) led to lower yields (73% and 69%, Table 1, entries 1 and 3). The result obtained at 16 mA cm^{-2} can probably be ascribed to a longer electrolysis time (which can lead to side reactions before the addition of propionic anhydride), while the one at 35 mA cm^{-2} can be ascribed to a lower current efficiency (with an increase of the ohmic component). The best result (97% chemical yield, Table 1, entry 2) was obtained using 25 mA cm^{-2} as current density and 1.0 F mol^{-1} of **1a** (which corresponds to a 97% current yield for this monoelectronic process that leads to the formation of the carbene; see Scheme 1). An increase in the number of Faradays per mol of **1a** not only is not necessary, but it leads to a lowering in the yields of **3aa**.

To investigate the scope and the synthetic utility of this method, the procedure was carried out using various saturated or unsaturated anhydrides and alkyl halides. *N*-Acylbenzoxazolones **3aa**–**3af** (Table 2, entries 1–6) and *N*-alkylbenzoxazolones **3ag**–**3ai** (Table 2, entries 7–9) were isolated in elevated yields. Moreover, to test the effectiveness and generality of this electrochemical method, the investigation (according to the optimized conditions, Table 1, entry 2), was extended to a large variety of substituted benzoxazol-2(3*H*)-ones **1a**–**1h**, to 1*H*-benzoimidazol-2-(3*H*)-one **1i**, benzoxazole-2(3*H*)-thione **1j** and benzothiazol-2-(3*H*)-one **1k**. To emphasize the usefulness of this methodology, propionic anhydride was chosen as acylant to give a prochiral methylene group for subsequent reactions.

As can be see in Table 2, benzoxazol-2(3*H*)-ones derivatives **3** were isolated in good or high yields, with the only exception of **3ba** (Table 2, entry 10), in which the methyl group in the ortho position has a too large steric hindrance and lowers the reactivity of the nitrogen anion. The presence of a thiocarbonyl group in the structure instead of C=O gave the corresponding 1-(2-thioxobenzo[*d*]oxazol-3(2*H*)-yl)propan-1-one **3ja** in low yield (Table 2, entry 18). The reaction worked very well with 1*H*-benzoimidazol-2-(3*H*)-one **1i**, but when a sulfur atom was present in the heterocyclic structure, the corresponding 3-propionylbenzo[*d*]-thiazol-2(3*H*)-one **3ka** was isolated in negligible yields (Table 2, entry 19). Secondary effects of the nature of the substituents on the phenyl ring on the yields of isolated products have been evinced. For example, the presence of an electron-withdrawing group as $-NO_2$, on the aromatic ring lowered the reactivity of the nitrogen anion and 6-nitro-3-propionylbenzo[*d*]oxazol-2(3*H*)-one **3ha** was obtained in 55% yield (Table 2, entry 16).

The *N*-acyl derivatives of benzoxazolones and benzothiazolone can be modified at high temperature in a 'Fries-like' rearrangement to give 6-acyl-2(3*H*)-benzoxazolones and 6-acyl-2(3*H*)benzothiazole derivatives,[19] which posses potent in vivo anticonvulsant and in vitro antiviral activities. Besides, the N-alkylation of **1a** represents an important result because many interesting medicinal compounds, bearing a short chain on 3-position of benzoxazolone structure, show a high degree of protection again maximal electroshock-induced seizures.[5]

The electrochemical deprotonation of benzoxazolone **1f**, followed by the addition of ethyl iodide, led to the isolation of the corresponding 5-chloro-3-ethylbenzo[*d*]oxazol-2(3*H*)-one **3fh** in a very high yield (see Scheme 2). This compound is very important due to its activity as modulator of SK_{Ca}, IK_{Ca} and BK_{Ca} channels[11] and it was synthesized in 47% yield by reaction of **1f** with sodium hydride and bromoethane in anhydrous DMF.

Scheme 2.

The major advantage of the use of ionic liquids as a reaction medium is that the solvent can be easily recovered and recycled in subsequent runs. The reusability of the reaction medium was tested in the N-acylation with propionic anhydride **2a** of benzo[*d*]oxazol-2(3*H*)-one **1a**; the results are presented in Table 3.[14] After each run, 3-propionylbenzo[*d*]oxazol-2(3*H*)-one **3aa** was removed by diethyl ether extraction and RTIL was kept under vacuum for 1 h, then reused for the following cycle (up to five). As can be seen, all the cycles furnished excellent to good yields.

In conclusion, according to the topical purpose for simple experimental conditions, the N-acylation/alkylation of benzoxazol-2(3*H*)-ones, benzothiazol-2-(3*H*)-one and 1*H*-benzoimidazol-2-(3*H*)-one have been carried out via galvanostatic electrolyses of ionic liquid solutions containing the starting substrates at room temperature. An electrogenerated carbene, resulting from the cathodic reduction of the ionic liquid, may be indicated as the base involved in the deprotonation. The derivatives obtained after addition of saturated or unsaturated anhydrides or alkylants gave the expected products in good to excellent yields. Effective solvent recycling has been shown and the simplicity of the system (basic electrochemical equipment, RTILs as solvent/supporting electrolyte/probase, room temperature) makes these results of high interest for electrochemical and organic synthesis.

Table 3
Recyclability of BMIM-BF_4 in N-acylation of benzo[*d*]oxazol-2(3*H*)-one **1a** with propionic anhydride **2a**[a]

Entry	Cycle	**1a** [%] recovered	Isolated **3aa** yield [%]
1	First	—	97
2	Second	—	98
3	Third	tr	94
4	Fourth	12	81
5	Fifth	30	69

[a] Electrolyses carried out under galvanostatic conditions. Divided cell, Pt anode and cathode, I=25 mA cm^{-2}, 1 F mol^{-1} of **1a**, under N_2, room temperature.

3. Experimental

3.1. Electrochemical set up and typical procedure

Preparative electrolyses were carried out at room temperature in a two-compartment cell separated by a sintered glass disk. A solution of ionic liquids (1.5 mL) containing 2(3*H*)-benzoxazolone (0.5 mmol) was electrolyzed under galvanostatic control (I=25 mA cm^{-2}) under N_2. After the consumption of 1.0 F mol^{-1} of benzoxazolone, the current was switched off and the anhydride or alkyl halide (0.5 mmol) was added to the cathodic solution, and the mixture was stirred at room temperature for 2 h. The catholite was extracted with diethyl ether (3×10 mL); the solvent was removed from the combined organic layers under reduced pressure, and the residue was purified by flash chromatography (hexane–ethyl acetate 8:2) affording the corresponding *N*-acyl derivative.

The following compounds were prepared according to this procedure.

3.1.1. 3-Acetylbenzo[d]oxazol-2(3H)-one **3aa**[8,19]

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.96–7.92 (m, 1H), 7.19–7.08 (m, 3H), 2.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 169.4, 151.4, 142.2, 127.6, 125.3, 124.8, 115.9, 109.8, 24.8. GC–MS (EI) m/z: $M^{+\bullet}$ absent, 162 (26%), 161 (64%), 145 (21%), 106 (2%), 43 (100%). Anal. Calcd for $C_9H_7NO_3$: C, 61.02; H, 3.98; N, 7.91. Found: C, 61.08; H, 4.01; N, 7.88.

3.1.2. 3-Propionylbenzo[d]oxazol-2(3H)-one **3ab**[19]

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.02–7.98 (m, 1H), 7.22–7.14 (m, 3H), 3.07 (q, 2H, J=7.3 Hz), 1.23 (t, 3H, J=7.3 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 173.2, 151.2, 142.1, 127.7, 125.0, 124.6, 115.8, 109.6, 30.3, 7.9. GC–MS (EI) m/z: 191 ($M^{+\bullet}$, 70%), 135 (100%), 106 (37%), 57 (100%). Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.90; H, 4.77; N, 7.32.

3.1.3. 3-Butyrylbenzo[d]oxazol-2(3H)-one **3ac**[20]

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.02–7.99 (m, 1H), 7.20–7.15 (m, 3H), 3.02 (t, 2H, J=7.2 Hz), 1.75 (sextet, 2H, J=7.2 Hz), 1.00 (t, 3H, J=7.2 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 172.4, 151.2, 142.2, 127.8, 125.0, 124.6, 115.8, 109.6, 38.4, 17.3, 13.5. GC–MS (EI) m/z: 206 ($M^{+\bullet}$+1, 21%), 205 ($M^{+\bullet}$, 69%), 135 (100%), 106 (55%), 43 (100%). Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.40; H, 5.44; N, 6.84.

3.1.4. (E)-3-But-2-enoylbenzo[d]oxazol-2(3H)-one **3ad**

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.05–8.00 (m, 1H), 7.35–7.31 (m, 2H), 7.22–7.15 (m, 3H), 2.02–1.99 (m, 3H). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 163.9, 151.1, 149.2, 142.2, 128.0, 125.0, 124.6, 121.9, 116.0, 109.6, 18.6. GC–MS (EI) m/z: 203 ($M^{+\bullet}$, 3%), 135 (4%), 106 (1%), 69 (100%), 41 (21%), 39 (6%). Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.08; H, 4.50; N, 6.86.

3.1.5. 3-(2-Chloroacetyl)benzo[d]oxazol-2(3H)-one **3ae**

^{1}H NMR (acetone-d_6, 200 MHz): δ 8.02–7.89 (m, 1H), 7.35–7.33 (m, 3H), 5.03 (s, 2H). ^{13}C NMR (acetone-d_6, 50.3 MHz): δ 170.7,

156.2, 148.0, 133.0, 130.7, 130.0, 120.4, 115.1, 49.6. GC–MS (EI) *m*/*z*: 213 ($M^{+\bullet}$+2, 30%), 211 ($M^{+\bullet}$, 89%), 135 (100%), 106 (15%). Anal. Calcd for $C_9H_6ClNO_3$: C, 51.08; H, 2.86; N, 6.62. Found: C, 51.12; H, 2.90; N, 6.60.

3.1.6. 3-Benzoylbenzo[d]oxazol-2(3H)-one ***3af***[8,19]

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.86–7.76 (m, 3H), 7.66–7.59 (m, 1H), 7.52–7.45 (m, 2H), 7.29–7.24 (m, 3H). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 171.6, 167.6, 143.9, 142.7, 133.5, 132.1, 129.5, 128.3, 125.8, 125.2, 124.7, 115.0, 110.1. GC–MS (EI) *m*/*z*: 239 ($M^{+\bullet}$, 3%), 134 (1%), 106 (29%), 105 (100%), 77 (97%), 51 (11%). Anal. Calcd for $C_{14}H_9NO_3$: C, 70.29; H, 3.79; N, 5.86. Found: C, 70.33; H, 3.81; N, 5.86.

3.1.7. Ethyl 5-(2-oxobenzo[d]oxazol-3(2H)-yl)pentanoate ***3ag***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.15–7.02 (m, 3H), 6.94–6.90 (m, 1H), 4.04 (q, 2H, *J*=7.2 Hz), 3.78 (t, 2H, *J*=6.4 Hz), 2.30 (t, 2H, *J*=6.4 Hz), 1.81–1.61 (m, 4H), 1.18 (t, 3H, *J*=7.2 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 172.9, 154.4, 142.6, 131.0, 123.6, 122.2, 109.8, 108.1, 60.3, 41.7, 33.4, 27.0, 21.8, 14.0. GC–MS (EI) *m*/*z*: 264 ($M^{+\bullet}$+1, 24%), 263 ($M^{+\bullet}$, 56%), 218 (32%), 190 (16%), 176 (18%), 161 (100%), 148 (56%), 135 (56%), 129 (53%), 101 (61%). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.93; H, 6.56; N, 5.30.

3.1.8. 3-Ethylbenzo[d]oxazol-2(3H)-one ***3ah***[21]

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.24–7.03 (m, 3H), 6.97–6.94 (m, 1H), 3.86 (q, 2H, *J*=7.2 Hz), 1.35 (t, 3H, *J*=7.2 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 154.3, 142.7, 130.8, 123.7, 122.2, 109.9, 108.1, 37.1, 12.9. GC–MS (EI) *m*/*z*: 164 ($M^{+\bullet}$+1, 6%), 163 ($M^{+\bullet}$, 100%), 148 (55%), 135 (62%), 91 (13%). Anal. Calcd for $C_9H_9NO_2$: C, 66.25; H, 5.56; N, 8.58. Found: C, 66.30; H, 5.60; N, 8.58.

3.1.9. 3-Methylbenzo[d]oxazol-2(3H)-one ***3ai***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.19–7.07 (m, 3H), 6.95–6.91 (m, 1H), 3.37 (s, 1H). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ154.5, 142.62, 131.70, 123.79, 122.43, 109.87, 108.01, 28.03. GC–MS (EI) *m*/*z*: 150 ($M^{+\bullet}$+1, 7%), 149 ($M^{+\bullet}$, 100%), 120 (13%), 93 (6%). Anal. Calcd for $C_8H_7NO_2$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.45; H, 4.77; N, 9.37.

3.1.10. 4-Methyl-3-propionylbenzo[d]oxazol-2(3H)-one ***3bb***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.17–6.99 (m, 3H), 3.17 (q, 2H, *J*=7.3 Hz), 2.36 (s, 3H), 1.28 (t, 3H, *J*=7.3 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 173.1, 152.0, 143.3, 127.9, 126.5, 126.3, 125.2, 107.4, 31.1, 21.2, 8.7. GC–MS (EI) *m*/*z*: 205 ($M^{+\bullet}$, 2%), 149 (100%), 121 (2%), 57 (23%). Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.40; H, 5.40; N, 6.82.

3.1.11. 5-Methyl-3-propionylbenzo[d]oxazol-2(3H)-one ***3cb***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.84 (s, 1H), 7.10–6.89 (m, 3H), 3.87 (q, 2H, *J*=7.3 Hz), 2.36 (s, 3H), 1.23 (t, 3H, *J*=7.3 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 173.4, 151.5, 140.2, 134.7, 127.6, 125.4, 116.3, 109.1, 30.3, 21.4, 7.9. GC–MS (EI) *m*/*z*: 205 ($M^{+\bullet}$, 14%), 150 (21%), 149 (100%), 57 (29%). Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.42; H, 5.42; N, 6.83.

3.1.12. 6-Methyl-3-propionylbenzo[d]oxazol-2(3H)-one ***3db***

^{1}H NMR (acetone-d_6, 200 MHz): δ 7.88 (d, 1H, *J*=8.1 Hz), 7.14 (s, 1H), 7.08 (d, 1H, *J*=8.1 Hz), 3.09 (q, 2H, *J*=7.3 Hz), 2.38 (s, 3H), 1.20 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (acetone-d_6, 50.3 MHz): δ 174.0, 152.2, 143.4, 136.1, 126.8, 125.7, 116.0, 110.9, 30.6, 21.4, 8.2. GC–MS (EI) *m*/*z*: 205 ($M^{+\bullet}$, 24%), 150 (65%), 149 (100%), 57 (92%). Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found $C_{11}H_{11}NO_3$: C, 64.44; H, 5.43; N, 6.81.

3.1.13. 5-Fluoro-3-propionylbenzo[d]oxazol-2(3H)-one ***3eb***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.83 (dd, 1H, *J*=8.5, 2.7 Hz), 7.13 (dd, 1H, *J*=9.0, 4.3 Hz), 6.93 (ddd, 1H, *J*=9.0, 9.0, 2.7 Hz), 3.10 (q, 2H, *J*=7.2 Hz), 1.26 (t, 3H, *J*=7.2 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 173.1, 159.5 (d, ^1J=240.9 Hz), 151.3, 138.2 (d, ^4J=2.3 Hz), 128.2 (d, ^3J=13.4 Hz), 111.4 (d, ^2J=24.9 Hz), 110.2 (d, ^3J=9.3 Hz), 104.5 (d, ^2J=30.9 Hz), 30.3, 7.8. GC–MS (EI) *m*/*z*: 210 ($M^{+\bullet}$+1, 23%), 209 ($M^{+\bullet}$, 81%), 153 (100%), 124 (71%), 57 (100%), 29 (91%). Anal. Calcd for $C_{10}H_8FNO_3$: C, 57.42; H, 3.85; N, 6.70. Found: C, 57.48; H, 3.88; N, 6.68.

3.1.14. 5-Chloro-3-propionylbenzo[d]oxazol-2(3H)-one ***3fb***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.02 (d, 1H, *J*=2.0 Hz), 7.37 (dd, 1H, *J*=8.6, 2.0 Hz), 7.07 (d, 1H, *J*=8.6 Hz), 3.06 (q, 2H, *J*=7.3 Hz), 1.23 (t, 3H, *J*=7.3 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 173.0, 150.8, 140.6, 130.2, 128.4, 125.0, 116.3, 110.5, 30.3, 7.8. GC–MS (EI) *m*/*z*: 227 ($M^{+\bullet}$+2, 2%), 225 ($M^{+\bullet}$, 7%), 171 (29%), 169 (73%), 57 (100%), 29 (60%). Anal. Calcd for $C_{10}H_8ClNO_3$: C, 53.23; H, 3.57; N, 6.21. Found: C, 53.28; H, 3.61; N, 6.19.

3.1.15. 5-Bromo-3-propionylbenzo[d]oxazol-2(3H)-one ***3gb***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.25 (d, 1H, *J*=2.0 Hz), 7.37 (dd, 1H, *J*=8.5, 2.0 Hz), 7.07 (d, 1H, *J*=8.5 Hz), 3.10 (q, 2H, *J*=7.2 Hz), 1.26 (t, 3H, *J*=7.2 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 172.9, 150.7, 141.1, 128.7, 127.9, 118.9, 117.3, 110.9, 30.3, 7.8. GC–MS (EI) *m*/*z*: 271 ($M^{+\bullet}$+2, 4%), 269 ($M^{+\bullet}$, 4%), 215 (44%), 213 (43%), 57 (100%), 29 (43%). Anal. Calcd for $C_{10}H_8BrNO_3$: C, 44.47; H, 2.99; N, 5.19. Found: C, 44.51; H, 3.01; N, 5.21.

3.1.16. 6-Nitro-3-propionylbenzo[d]oxazol-2(3H)-one ***3hb***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.21 (d, 2H, *J*=1.4 Hz), 8.09 (d, 2H, *J*=1.2 Hz), 3.14 (q, 2H, *J*=7.2 Hz), 1.28 (t, 3H, *J*=7.2 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 172.9, 150.5, 145.0, 141.9, 132.6, 121.1, 115.8, 106.0, 30.6, 7.8. GC–MS (EI) *m*/*z*: 236 ($M^{+\bullet}$, 2%), 164 (2%), 106 (2%), 57 (100%), 29 (15%). Anal. Calcd for $C_{10}H_8N_2O_5$: C, 50.85; H, 3.41; N, 11.86. Found: C, 50.89; H, 3.46; N, 11.85.

3.1.17. 1-Propionyl-1H-benzo[d]imidazol-2(3H)-one ***3ib***

^{1}H NMR (acetone-d_6, 200 MHz): δ 10.1 (br s, 1H), 8.13–8.08 (m, 1H), 7.21–7.04 (m, 3H), 3.13 (q, 2H, *J*=7.3 Hz), 1.22 (t, 3H, *J*=7.3 Hz). ^{13}C NMR (acetone-d_6, 50.3 MHz): δ 175.1, 153.4, 129.9, 128.7, 125.1, 122.6, 116.2, 109.8, 31.2, 8.6. GC–MS (EI) *m*/*z*: 190 ($M^{+\bullet}$, 5%), 135 (11%), 134 (100%), 106 (13%), 57 (3%). Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.21; H, 5.35; N, 14.74.

3.1.18. 1-(2-Thioxobenzo[d]oxazol-3(2H)-yl)propan-1-one ***3jb***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.10–8.05 (m, 1H), 7.30–7.26 (m, 3H), 3.50 (q, 2H, *J*=7.3 Hz), 1.30 (t, 3H, *J*=7.3 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 178.8, 174.9, 148.6, 130.0, 126.0, 125.5, 116.4, 109.6, 33.1, 8.3. GC–MS (EI) *m*/*z*: 207 ($M^{+\bullet}$, 2%), 179 (5%), 151 (100%), 135 (5%), 57 (23%). Anal. Calcd for $C_{10}H_9NO_2S$: C, 57.95; H, 4.38; N, 6.76. Found: C, 57.99; H, 4.41; N, 6.74.

3.1.19. 3-Propionylbenzo[d]thiazol-2(3H)-one ***3kb***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.27 (d, 1H, *J*=7.9 Hz), 7.34–7.18 (m, 3H), 3.12 (q, 2H, *J*=7.3 Hz), 1.25 (t, 3H, *J*=7.3 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 175.0, 170.9, 134.9, 126.9, 125.3, 121.9, 117.7, 32.6, 8.5. GC–MS (EI) *m*/*z*: 207 ($M^{+\bullet}$, 6%), 151 (100%), 123 (8%), 57 (43%). Anal. Calcd for $C_{10}H_9NO_2S$: C, 57.95; H, 4.38; N, 6.76. Found: C, 58.01; H, 4.44; N, 6.76.

3.1.20. 3-Methyl-1-propionylimidazolium chloride[22]

^{1}H NMR ($CDCl_3$, 200 MHz): δ 11.06 (s, 1H), 7.65 (s, 1H), 6.98 (s, 1H), 6.80 (s, 1H), 3.60 (s, 1H), 2.22 (q, 2H, *J*=7.6 Hz), 1.02 (t, 3H, *J*=7.6 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 178.2, 137.3, 127.0, 120.3, 33.6, 27.9, 9.2. Anal. Calcd for $C_7H_{10}ClN_2O$: C, 48.42; H, 5.81; N, 16.13. Found: C, 48.49; H, 5.86; N, 16.11.

3.1.21. 5-Chloro-3-ethylbenzo[d]oxazol-2(3H)-one ***3fh***

^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.25–7.03 (m, 3H), 6.95 (s, 1H), 3.85 (q, 2H, *J*=7.2 Hz), 1.34 (t, 3H, *J*=7.2 Hz). ^{13}C NMR ($CDCl_3$, 50.3 MHz):

δ 153.9, 141.08, 131.77, 129.17, 121.99, 110.66, 108.55, 37.28, 12.77. GC–MS (EI) m/z: 199 ($M^{+\bullet}$, +2, 82%), 197 ($M^{+\bullet}$, 100%), 171 (57%), 169 (100%), 113 (57%). Anal. Calcd for $C_9H_8ClNO_2$: C, 54.70; H, 4.08; N, 7.09. Found: C, 54.75; H, 4.01; N, 7.08.

3.1.22. General remarks

Electrochemical experiments were carried out using a glass two-compartment home-made cell. Anolyte and catholyte (ca. 1.5 mL each) were separated through a glass disk (porosity 5). The electrode surface areas were 1 cm^2 for the cathode Pt spiral electrode (wire, 99.9%) and 0.8 cm^2 for the anode Pt spiral electrode (wire, 99.9%).

3.1.23. Chemicals

All reagents were commercially available and used as received. Ionic liquids were commercially available and used as pure compounds.

Acknowledgements

We thank Mr. M. Di Pilato for his contribution to the experimental part of this work. This work was supported by research grants from MURST (Prin 2006) and CNR, Roma, Italy.

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